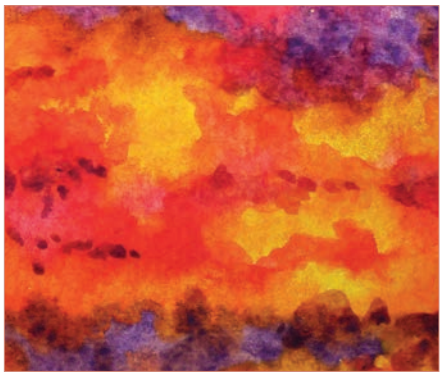

A Case of Vancomycin-induced Acute Generalized Exanthematous Pustulosis Confirmed by Patch Testing

ABSTRACT

Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous drug reaction that presents with the rapid onset of disseminated pustules, erythema, and edema. It is commonly associated with pristinamycin and aminopenicillins, but a few cases of vancomycin induced AGEP have been reported. Here, we describe a patient who presented with AGEP 12 hours following vancomycin administration, and had an atypical clinical course, with the AGEP persisting for weeks. Vancomycin was confirmed to be the etiologic agent with patch testing, a modality with growing evidence for utility in drug-induced reaction cases.

KEY WORDS: Vancomycin, acute generalized exanthematous pustulosis, cutaneous drug reaction

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Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous drug reaction that presents with the rapid onset of disseminated pustules, erythema, and edema. The rash classically begins on the face and then spreads to the limbs and trunk. Following resolution, an annular pattern of desquamation can persist.[1] Antibiotics are the most common cause of AGEP, with pristinamycin, aminopenicillins, macrolides, and sulfonamides being the most common offenders.[2,3] Other drugs, such as terbinafine, hydroxychloroquine, and diltiazem, can also cause the reaction.[2] The use of vancomycin is extremely common in hospitals, yet a review of the literature shows only four previously reported cases of vancomycin induced AGEP.[1,3–5] We present a patient with a low pre-test probability association with vancomycin but confirmed via patch testing.

CASE REPORT

A 70-year-old woman who had received a total knee replacement was hospitalized for prosthetic joint infection. Cephalexin was given initially, and, following lack of improvement, clindamycin was initiated, followed by vancomycin 36 hours later. Twelve hours following vancomycin administration, diffuse subcorneal pustules and erythema developed, with especially heavy involvement of the intertriginous regions (Figure 1). A diagnosis of AGEP was made, and, based on the time course and epidemiology, was believed to be due to the clindamycin. A prednisone taper was given, and she was scheduled for follow up. At her follow-up appointment one week later, the rash had further spread, now involving her face. Cyclosporine was initiated. At a return visit three weeks later, the rash had completely resolved. Patch testing was performed, which showed reactivity to vancomycin but not clindamycin or cephalosporins (Figure 2).

DISCUSSION

At the cellular level, AGEP can be classified as a T-cell dependent type IV hypersensitivity reaction. CD8 T cells, sensitized by exposure to the offending drug, migrate to the skin, where they lyse keratinocytes, forming subcorneal vesicles. CD4 helper T cells, also sensitized by the drug, then release inflammatory cytokines, including IL-8a and IL-17, which recruit neutrophils. The neutrophils then proceed to convert the subcorneal vesicles into the characteristic pustules present in the disease.[2,6] The clinical course is classically very rapid, with an onset within a day of exposure and resolution usually occurring several days

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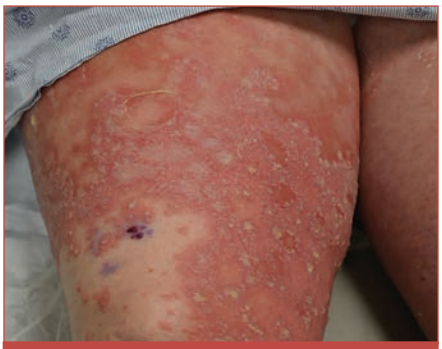

FIGURE 1. Diffuse pustules on an erythematous base, consistent with a diagnosis of AGEP

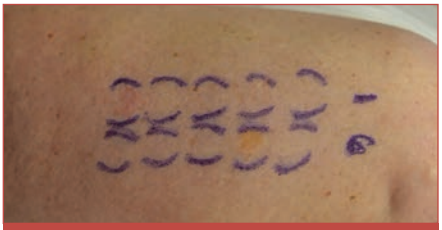

FIGURE 2. Positive patch test to Vancomycin

following withdrawal of the offending drug.

Confirming the drug that caused AGEP can be difficult, as hospitalized patients are often exposed to a multitude of drugs. In our case, clindamycin was felt to have a better time course, in addition to often being reported as the most common etiology for AGEP in the hospitalized setting.[7] In severe reactions, such as AGEP, trials of systemic exposure to the drugs to discover the causative agent would be prohibitively dangerous. In recent years, evidence for patch testing to confirm the causative drug has been growing. Traditionally, patch testing has been utilized to identify contact irritants and allergens, such as fragrances, metals, and topical antibiotics. There is evidence, however, that it can be used for reactions to systemic drugs as well.[8,9] It is theorized that T cells that reside in the skin may also undergo sensitization during a drug reaction, and, therefore, will react similarly when exposed cutaneously to the offending drug. Interestingly, the histopathology of positive patch tests often mirrors that of the initial drug reaction.[8] One recent study that conducted patch testing for drugs suspected as a cause of cutaneous drug reactions found a positive patch result to the suspected drug in 18.1 percent of cases of AGEP.[8] Another study, however, had a positive patch result in 58 percent of cases of AGEP.[9] Many factors were cited as possible causes of the variable sensitivity, including inappropriate drug penetration through the epidermis, reactions due to drug metabolites rather than drug itself, and inadequacy of the vehicle carrying the drug.[8] In one of the previous cases of vancomycin-induced AGEP, vancomycin was also confirmed to be the causative agent via positive patch test results.[4]

The confirmation via patch testing for sensitivity to vancomycin represents completing evidence that this truly was the cause of the AGEP, despite early time course and low frequency of reports. This adds to the growing evidence that vancomycin can cause this reaction. This reaction, while rare, is extremely clinically significant, as vancomycin is commonly used in the hospital setting and patients requiring the drug are often very ill. Recognition of the drug responsible for an episode of AGEP is critical, as future exposures to the drug will lead to repeated and possibly dangerous reactions. Despite its variable sensitivity, patch testing is very safe, and may be a useful method to aid in the identification of the drug responsible adverse cutaneous reactions, especially when that reaction is rare, such as vancomycin-induced AGEP.

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